

**Table S1. Cytokines, chemokines and growth factors included in the analysis**

Cytokine	Abbreviation	Minimum detected cytokine concentration (pg/ml)
Interferon- $\alpha$ 2	IFN $\alpha$ 2	8.43
Interleukin-3	IL-3	13.68
Leukemia inhibitory factor	LIF	1.87
Chemokine (C-C motif) ligand 7	CCL7	3.19
Interleukin-18	IL-18	64.33
KIT ligand	KITLG	32.38
Chemokine (C-X-C motif) ligand 12	CXCL12	30.62
Interleukin-1 $\alpha$	IL-1 $\alpha$	0.01
Hepatocyte growth factor	HGF	220.85
Colony stimulating factor-1	CSF1	0.06
Interleukin-1 receptor antagonist	IL-1Ra	52.29
Interleukin-8	IL-8	1.09
Chemokine (C-X-C motif) ligand 10	CXCL10	787.06
Nerve growth factor	NGF	1.41
Chemokine (C-C motif) ligand 27	CCL27	255.11
Interleukin 2 receptor a	IL-2Ra	101.37
Interleukin-12p40	IL-12p40	43.34
Interleukin-6	IL-6	3.92
Lymphotoxin a	LTA	0.07
Chemokine (C-X-C motif) ligand 9	CXCL9	25.19
Interleukin-10	IL-10	1.6
Interleukin-5	IL-5	0.12
C-type lectin domain family 11 member A	CLEC11A	10,961.07
Interleukin-15	IL-15	1.3
Colony stimulating factor 3	CSF3	1.28
Platelet-derived growth factor $\beta$ polypeptide	PDGF $\beta$	14.04
Chemokine (C-C motif) ligand 4	CCL4	34.65
Chemokine (C-C motif) ligand 2	CCL2	0.15
Interleukin-9	IL-9	0.06
Macrophage migration inhibitory factor	MIF	89.27
Chemokine (C-X-C motif) ligand 1	CXCL1	57.92
Interleukin-2	IL-2	0.66
Interferon- $\gamma$	IFN $\gamma$	9.66
Tumor necrosis factor (ligand) superfamily member 10	TNFSF10	58.59
Chemokine (C-C motif) ligand 11	CCL11	16.01
Chemokine (C-C motif) ligand 5	CCL5	292.83
Interleukin-16	IL-16	56.06
Interleukin-1 $\beta$	IL-1 $\beta$	0.23
Interleukin-4	IL-4	0.31
Interleukin-7	IL-7	0.76

Interleukin-12	IL-12	2.45
Interleukin-13	IL-13	0.6
Interleukin-17	IL-17	3.25
Fibroblast growth factor 2	FGF2	0.7
Colony stimulating factor 2	CSF2	0.3
Tumor necrosis factor	TNF	0.06
Vascular endothelial growth factor A	VEGFA	1.34
Chemokine (C-C motif) ligand 3	CCL3	1.61

**Table S2. Serum cytokine concentrations during fatal and nonfatal iNTS disease**

	Median (IQR) cytokine concentration (pg/ml)			
	Survived	Died	$P_{\text{unadjusted}}$	$P_{\text{adjusted}}$
HGF	1,659 (1,035-2,697)	5,390 (2,801-7,115)	$1.3 \times 10^{-5}$	$6.4 \times 10^{-4}$
IL-8	34.1 (26.1-57.9)	131.3 (66.4-206.2)	$7.3 \times 10^{-5}$	$3.4 \times 10^{-3}$
IL-1Ra	697.7 (251.7-1,457.6)	5,339.9 (1,051.7-9,819.8)	$2.0 \times 10^{-4}$	$9.2 \times 10^{-3}$
IL-18	1,097 (616-1,795)	2,684 (1,967-4,948)	$2.2 \times 10^{-4}$	0.01
IL-3	299.4 (166.2-437.1)	537.9 (411.1-716.1)	$3.4 \times 10^{-4}$	0.02
IL-1 $\alpha$	2.4 (1.4-3.3)	4.0 (3.3-4.5)	$3.6 \times 10^{-4}$	0.02
LIF	28.8 (4.2-54.4)	72.3 (52.2-94.9)	$3.8 \times 10^{-4}$	0.02
IFN $\alpha$ 2	154.6 (119.4-188.6)	220.3 (205.2-232.9)	$4.1 \times 10^{-4}$	0.02
CXCL12	251.1 (184.9-305.4)	408.8 (283.4-540.6)	$4.5 \times 10^{-4}$	0.02
CCL7	45.9 (28.6-63.6)	89.6 (72.2-93.4)	$8.0 \times 10^{-4}$	0.03
KITLG	176.7 (120.8-250.8)	322.5 (233.7-387.2)	$8.3 \times 10^{-4}$	0.03
CSF1	38.1 (27.2-60.7)	104.0 (48.1-158.0)	$1.1 \times 10^{-3}$	0.04
LTA	5.5 (3.4-7.7)	8.4 (6.9-11.4)	$1.8 \times 10^{-3}$	0.07
CCL27	1,072 (826-1,391)	1,680 (1,290-1,914)	$2.1 \times 10^{-3}$	0.07
NGF	9.0 (6.6-13.5)	15.8 (12.0-18.5)	$2.6 \times 10^{-3}$	0.09
IL-16	264.0 (182.3-359.2)	402.1 (294.8-574.3)	$2.6 \times 10^{-3}$	0.09
TNFSF10	371.1 (254.4-492.6)	555.9 (440.5-626.9)	$3.8 \times 10^{-3}$	0.12
CCL4	230.8 (127.4-317.3)	340.9 (261.8-626.9)	$5.2 \times 10^{-3}$	0.16
PDGF $\beta$	4,131.3 (2,350.7-8,176.6)	864.7 (328.6-3,933.6)	0.01	0.31
IL-12p40	649.8 (444.6-957.2)	956.9 (626.9-1,313.4)	0.02	0.45
IL-6	38.9 (20.4-91.6)	103.1 (41.2-264.1)	0.02	0.51
CCL5	8,515 (6,098-11,082)	4,390 (1,803-10,793)	0.02	0.59
IL-2Ra	916 (539-1,453)	1,236 (1,025-3,069)	0.03	0.68
CCL2	14.8 (5.6-30.4)	32.6 (16.7-62.3)	0.03	0.70
IL-15	13.0 (1.7-23.9)	24.5 (13.4-31.8)	0.03	0.79
MIF	727.9 (464.7-1,128.7)	1,310.7 (641.9-2,126.7)	0.04	0.83

CCL11	166.5 (97.9-252.4)	247.3 (150.2-494.4)	0.04	0.85
CSF3	41.8 (22.9-63.4)	53.4 (35.2-399.5)	0.10	1.00
CXCL1	376.5 (241.1-641.7)	294.0 (134.2-436.8)	0.14	1.00
IL-5	0.8 (0.1-2.0)	0.1 (0.1-0.9)	0.15	1.00
CCL3	5.5 (1.6-11.3)	10.6 (2.4-16.1)	0.16	1.00
IL-10	14.5 (7.2-32.5)	18.7 (9.8-59.6)	0.16	1.00
CXCL9	11,656 (6,518-23,796)	18,431 (9,093-31,361)	0.24	1.00
IL-17	72.0 (38.2-143.7)	92.0 (39.7-217.4)	0.25	1.00
CXCL10	16,445 (9,223-29,322)	22,891 (17,663-41,272)	0.28	1.00
VEGFa	102.6 (52.8-150.3)	73.2 (13.7-148.2)	0.33	1.00
FGF2	23.5 (10.0-42.8)	16.4 (9.2-38.7)	0.39	1.00
CSF2	12.9 (0.3-25.1)	14.7 (5.1-49.5)	0.43	1.00
IL-12p70	39.2 (24.4-61.3)	38.9 (14.1-55.7)	0.46	1.00
TNF	5.5 (0.1-26.4)	2.7 (0.1-17.6)	0.57	1.00
IFN $\gamma$	393.1 (247.7-644.3)	325.1 (233.2-717.5)	0.67	1.00
IL-9	30.8 (15.9-51.9)	21.8 (16.3-64.2)	0.86	1.00
CLEC11a	61,008 (42,222-108,227)	74,930 (42,128-100,094)	0.86	1.00
IL-4	2.5 (1.5-3.7)	2.1 (1.5-3.1)	0.89	1.00
IL-7	6.1 (3.8-9.1)	6.6 (3.5-9.2)	0.90	1.00
IL-1 $\beta$	1.8 (0.4-3.3)	1.4 (0.2-4.4)	0.92	1.00
IL-13	6.9 (2.1-12.3)	8.4 (1.9-12.1)	0.93	1.00
IL-2	11.6 (5.9-20.8)	11.0 (3.7-33.7)	0.98	1.00

Data from 108 children (14 died, 94 survived) are included in the analysis. Significance testing is with Mann-Whitney U tests, with  $P$  values adjusted for multiple comparisons with Holm step-down corrections. Serum cytokines concentrations significantly altered in fatal cases of iNTS disease ( $P_{\text{adjusted}} < 0.05$ ) are highlighted in bold. IQR, interquartile range.

**Table S3. Logistic regression model of iNTS disease mortality including principal components of acute serum cytokine concentrations**

	Adjusted Odds Ratio (95% confidence interval) for mortality	P
PC1 <sub>mortality</sub>	1.53 (0.44-6.33)	0.459
PC2 <sub>mortality</sub>	<b>4.04 (1.40-15.10)</b>	<b>0.004</b>

Data from 108 children (14 died, 94 survived) are included in the model. PC, principal component.

**Table S4. Logistic regression model of iNTS disease mortality including the mortality-associated principal component of cytokine concentrations and NTS-associated comorbidities**

	Adjusted Odds Ratio (95% confidence interval) for mortality	P
PC2 <sub>mortality</sub>	<b>5.11 (2.29-14.18)</b>	<b>3.6x10<sup>-4</sup></b>
HIV	2.14 (0.48-10.51)	0.320
Malnutrition	2.04 (0.34-11.25)	0.411

Data from 97 children (14 died, 83 survived) are included in the model. PC, principal component.

**Table S5. Linear regression model of peripheral blood neutrophil counts in acute iNTS disease**

	$\beta$ coefficient (95% CI)	P
<b>PC2<sub>mortality</sub></b>	<b>0.24 (0.02-0.47)</b>	<b>0.04</b>
Age	0.00 (-0.01-0.01)	0.66
Sex	0.38 (-0.06-0.81)	0.10
Severe malnutrition	0.13 (-0.38-0.65)	0.62
HIV infection	0.11 (-0.32-0.53)	0.63

Data from 52 children are included in the model. PC, principal component.